Adverse drug reactions: a hospital pharmacy-based reporting scheme

P. A. WINSTANLEY, L. E. IRVIN, J. C. SMITH, M. L'E. ORME & A. M. BRECKENRIDGE

Royal Liverpool Hospital Pharmacy and Department of Pharmacology and Therapeutics, The University of Liverpool, Liverpool L69 3BX

A pharmacy-based adverse drug reaction (ADR) reporting scheme, using pharmacists, nurses and medical practitioners as initiators of reports, was set up at the end of 1984 in the Royal Liverpool Hospital in order to encourage reporting. New reports were inspected at weekly intervals by a staff pharmacist, and a clinical pharmacologist. Reports were forwarded to the Committee on Safety of Medicines if the reaction was considered to be serious by the clinicians, or the ADR team or involved 'black triangle' drugs. The total number of ADR reports was increased eightfold by the introduction of the scheme (from 14 in 1984 to 76, 102 and 94 in 1985, 1986 and 1987 respectively), and this rate of reporting has been sustained.

Keywords adverse drug reaction reports hospital patients.

Introduction

The prevalence of adverse drug reactions (ADRs) in hospital in-patients has been estimated to be between 1.5 and 35% (Bennett & Lipman, 1977; O'Connor *et al.*, 1988), but few are reported to the Committee on Safety of Medicines (CSM) (Rawlins, 1988). This low level of ADR reporting is shared by the Royal Liverpool Hospital (RLH), which has an annual death-discharge rate of 28000 (Irvin *et al.*, 1987), but from where in 1984 only 14 reports were sent to the CSM. An ADR reporting scheme was therefore set up at the RLH at the end of 1984 to try to improve the situation.

Methods

Simple preliminary report forms (PRF) (Irvin *et al.*, 1987) were provided in each clinical area of the RLH. An ADR-team, comprising a staff pharmacist and a clinical pharmacologist, was set up to administer the scheme. Their functions included communication (with the reporter of the ADR, and with the CSM, using the yellow card system), collation of data and promotion of the scheme within the hospital. Yellow cards were sent to the CSM on all ADRs considered to

be serious by the clinicians involved, or the ADR-team and all those involving 'black triangle' drugs. The scheme was promoted by the use of posters, by presentation of data at hospital staff rounds and at introductory sessions for new house officers. Pharmacists and nurses were encouraged to initiate reports.

Prescription records were not available, but it was possible to calculate the number of 'defined daily doses' (DDDs) of each drug from dispensing records. This concept of DDDs permits a comparison of the consumption of different drugs in common physical units. However, use of the Nordic Drug Index (Nordic Council on Medicines, 1985) was not possible, since many of the products in use at RLH were not listed. Consequently DDDs were calculated using the British National Formulary from the mean of the highest and lowest recommended daily doses for each drug studied.

Results

Figure 1 shows the numbers of PRF and CSM yellow cards for each half year period between 1984 (the year prior to the introduction of the

Figure 1 The numbers of preliminary report forms and CSM yellow cards for each half year period from 1984. ■ total reports, ▨ CSM yellow cards.

scheme) and June 1988 inclusive. As shown in Figure 1, approximately 60% of ADRs reported on PRF were forwarded to the CSM. Those which were not forwarded to the CSM were usually well recognised, minor ADRs associated with long established drugs e.g. rashes with ampicillin. Ninety % of reports originated from in-patients and 10% from out-patients. Reports of ADR seemed to increase with age, as has been noted by others (Castleden & Pickles, 1988), and 64% of patients were aged ≥ 51 years.

Of the PRF returned over the seven 6 month periods of the Scheme, yellow cards were sent to the CSM on $64 \pm 7\%$. In the most recent 6 month period within the remit of the present report (Jan–July 1988) 33 yellow cards were sent to the CSM. Sixteen of these reported suspected reactions to 'black triangle' drugs (propofol, augmentin, lofeprimine, enalapril, captopril, ranitidine, ciprofloxacin, cyclosporin, isosorbide mononitrate, α -interferon, and diltiazem). None of these ADRs proved fatal, but three were judged to be serious or life-threatening: propofol – status epilepticus; lofeprimine – hepatitis; and cyclosporin – cardiomyopathy. Of

the yellow cards sent, in this same period, concerning drugs without a 'black triangle' almost all were considered to be serious, and included: bendrofluozide – thrombocytopenia; metformin – lactic acidosis; and trimethoprim – aplastic anaemia.

Of the ADRs reported under the scheme, eight in-patients died: five as a result of blood dyscrasia, two as a result of toxic epidermal necrolysis, and one as a result of hepatitis. The drugs incriminated in these fatal ADRs were flecainide, sulphasalazine, captopril, cotrimoxazole, penicillamine, ibuprofen, 5-fluorouracil, methotrexate, mianserin and vancomycin.

Table 1 shows the percentage of all ADRs reported, which were attributed to each of the major drug categories, and the percentage of these which were serious or life-threatening. Table 1 also shows the percentage of total DDDs for each of the therapeutic categories in one representative month of the scheme.

Over the seven 6 month periods of the scheme, the skin was the site of the ADR in $36.7 \pm 14.7\%$ of reports (mean $\pm$ s.d.), while the CNS was affected in $13.7 \pm 2.6\%$, the gastrointestinal system in $10.9 \pm 5.8\%$, the cardiovascular or

Table 1 % of all ADRs reported, and % of these which were serious

Drug category	% total ADRs	% serious ADRs	Drug usage
			(% of total DDD)
	#	@	*
Anti-infective	28.5 ± 5.9	26	9
Cardiovascular	21.6 ± 6.7	20	25
CNS drugs	11.6 ± 6.2	41	18.5
NSAID	5.1 ± 3.5	59	6
Analgesics	5.5 ± 3.1	14	5.5
GIT drugs	3.8 ± 1.5	17	11
Cytotoxic	2.1 ± 1.8	50	3
Miscellaneous	21.0 ± 5.1	33	22

For each 6 month period 1985–1988 inclusive; mean ± s.d.

@ Percentage of the total number of ADRs attributed to that drug category 1985–1988 inclusive.

* Defined daily doses calculated as described in text; data calculated for one month of the study period (October, 1987).

renal systems in $9.4 \pm 6.1\%$, the blood in $6.0 \pm 2.3\%$, the liver in $5.3 \pm 1.8\%$ and the respiratory system in $4.0 \pm 2.8\%$; miscellaneous other reactions accounted for $13.5 \pm 2.4\%$. ADR reports originated from medical practitioners (58%), pharmacists (40%) and nurses (2%). In terms of broad medical specialty, 38% of ADR reports involved patients under 'General Medicine' (including clinical pharmacology), 18% from 'General Surgery', 10% from Geriatric Medicine, 8% from Orthopaedic Surgery, 6% from Intensive Care, 1% from Dentistry and a further 19% from other specialities.

Discussion

The CSM yellow card system of ADR reporting in the United Kingdom has an important role in the monitoring of marketed drugs (Drugs and Therapeutics Bulletin, 1988), and has successfully identified many drug hazards. However reporting rates are low, particularly in hospital practice where serious ADRs are most commonly to be found (Rawlins, 1988). Reporting rates need to be increased in order to reduce chances of bias and provide an earlier warning of hazard. It is possible to estimate crudely the prevalence of ADRs in hospital patients (Bennett & Lipman, 1977; O'Connor *et al.*, 1988) and at RLH the actual number of ADRs reported to the CSM, prior to the introduction of the present scheme, was several orders of magnitude below this figure. The present scheme was set up primarily to improve reporting rates from this general hospital.

The possible benefits of involving pharmacists in the reporting of ADRs is a subject of much

current interest (Veitch & Talbot, 1985). Although the CSM's Working Party on ADR reporting (1985) did not recommend that pharmacists should report suspected ADRs directly to the CSM, it accepted that pharmacists should participate in work relating to ADRs. The present scheme employed the spontaneous reporting of ADRs by pharmacists, nurses and medical practitioners, to an ADR-team of staff pharmacist and clinical pharmacologist who met weekly. Since ward pharmacists scrutinised prescription sheets daily at the RLH, had direct interest in ADRs and had close contact with house officers of all disciplines, they were thought to be the staff most likely to initiate reports. Indeed, although pharmacists were reporters of only 40% of all ADRs, they were involved in many of those reports initiated by medical practitioners and nurses. Furthermore, although the ADR-team comprised both pharmacists and medical practitioners, the day-to-day collection of data and their six monthly collation was undertaken largely by the pharmacist, whose working pattern was found to be more conducive to this task. The role of the clinical pharmacologist was largely one of medical and pharmacological advice (particularly regarding relative severity of ADRs), together with liaison with medical colleagues and interpretation of case note records.

The total number of ADR reports within the RLH was increased eightfold by the present scheme, and has been maintained. Even so, it is likely that there is still considerable under-reporting. Further improvements in the reporting rate of ADRs in RLH would probably involve an increase in the size and time commitment of the ADR team; others have used a reporting fee

as an effective incentive (O'Connor *et al.*, 1988). However both of these measures require that more resources be made available, and this seems unlikely.

The patterns of ADRs seen in RLH show some interesting differences from those reported using the general CSM data. In particular, NSAIDs probably account for about 5% of all prescriptions in the UK, but cause about 25% of ADRs (Rawlins, 1988). In the present data, NSAIDs accounted for a very similar percentage of hospital drug usage, but were reported to be the cause of only $5.1 \pm 3.5\%$ of ADRs. It is not clear why fewer ADRs were reported due to NSAIDs in the present data. It may be that fewer occur, which may be due to the use of a hospital formulary, which mainly lists the better known NSAIDs. Interestingly, the proportion of serious ADRs as a percentage of the total was higher for NSAIDs (59%) than for any other drug category, and it may be that there was bias of reporting for NSAIDs in favour of the more

serious ADRs. Minor and well known ADRs to NSAIDs, such as dyspepsia, may have been considered unimportant and therefore not reported. On the other hand, anti-infective drugs, while representing only 9% of overall drug usage, were reported as the cause of 28.5% of ADRs. However, of these only 26% were serious events, the remainder being most commonly due to uncomplicated rashes.

In conclusion, this ADR reporting scheme has increased the total number of reports from the RLH eightfold, and the number forwarded to the CSM fivefold, at relatively little cost. The initiation of similar pharmacy-based reporting schemes in other hospitals should now be encouraged.

The authors would like to thank the Committee on Safety of Medicines for its financial support of this scheme, and Mr J. Hampson for his help in the preparation of the manuscript.

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(Received 25 November 1988,
accepted 21 February 1989)